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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/815,310 | 03/22/2001 | Gavin C. Hirst | BBC-072/B | 4602 |

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| EXAMINER | |
|---|---|
| HABTE, KAHSAY | |
| **ART UNIT** | **PAPER NUMBER** |
| 1624 | |

DATE MAILED: 02/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/815,310 | HIRST ET AL. | |
| | Examiner | Art Unit | |
| | Kahsay Habte, Ph. D. | 1624 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-114,116-120,124,125 and 127-138* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-114,116-120,124,125 and 127-138* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12 and 14*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 1-114, 116-120, 124-125 and 127-138.

Note that there are two claim 37 and claim 35 is missing. Instead of numbering the claims as 33, 34, 36, 37, 37, 38, the numbering of the claims is changed to 33-38 according to rule 1.126.

### *Response to Amendment*

2. Applicant's amendment filed 01/22/2004 in response to the previous Office Action (Paper No. 11) is acknowledged. Rejections of claims 1-138 under 35 U.S.C. § 112, first and second paragraph (Paper No. 11, paragraphs 3-4, 5a, 5c-5f and 5h-5i) have been obviated.

### *Abstract*

3. The abstract is still defective, because there is no definition for variable G. See previous Office Action.

### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 40 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for many of the diseases listed in claim 120, does not

reasonably provide enablement for an ocular condition, cancer, chronic inflammation, inflammatory bowel disease, Lyme disease, cardiovascular condition, stroke, human immunodeficiency virus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to understand the invention commensurate in scope with these claims. There has been recited in claim 40, a method of treating an ocular condition, cancer, chronic inflammation, inflammatory bowel disease, Lyme disease, cardiovascular condition, stroke, human immunodeficiency virus, but the specification is not enabled for such a scope.

There has been recited in claim 40 a method of treating ocular condition (all pathological abnormalities of the eye) in general, but the specification is not enabled for such a scope. This means that the compound will treat diseases of the eye generally. There are scores of such diseases, arising from all kinds of sources, such as trauma, pregnancy, leukemia, excess light (photoretinopathy), rubella, hypertension arising from nephrosclerosis, diabetes, exudates of the eye, increased blood viscosity arising from dysproteinemia, CMV infections, neovascularization, side effect of other drugs (toxic retinopathy), excess oxygen arising from treatment of premature birth, a sudden rise in venous pressure, and other causes as well. Further, these retinopathies take many and quite varied forms, including degeneration of the choroid, hemorrhages, microaneurysms, edema of the retina, occlusion of the central retinal vein, retinal ischemia, angiospasms of retinal arterioles, various glaucomas such as primary open-angle glaucoma, a neurodegenerative disorder, dilation of retinal veins, night blindness,

papilledema, various forms of macular degeneration, retinal detachment, retrolental fibroplasia, and many other problems.

Neuroretinitis is inflammation of the retina and optic nerve of the eye ("optic neuritis"). It is often idiopathic. It frequently arises secondary to some kind of infection, such as Hepatitis B, HSV, EBV, influenza A, mumps, Coxsackie B, TB, salmonella, Lyme disease, syphilis, leptospirosis, Histoplasmosis, Toxoplasmosis, toxocara, Sarcoidosis and cat-scratch disease. Treatment is thus to the underlying cause. For example, Diffuse unilateral subacute neuroretinitis (DUSN) arises from nematodes deep in the retina or in the subretinal space. Anthelminthic treatment is then used. When the origin is Toxoplasmosis, then anti-Toxoplasma medications such as Pyrimethamine.

Other eye inflammations include scleritis and episcleritis, inflammation of tissues on the sclera; choroiditis, inflammation of the middle coat (choroid) of the eyeball, and uveitis, which is inflammation of the parts of the eyes that make up the iris.

Preseptal cellulitis is inflammation of the tissues around the eye, and Orbital cellulitis is aninflammatory process involving the layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise from staphylococcus. Hence, these types of inflammations are treated with intravenous antibiotics.

The vast majority of these are not treatable by any pharmaceutical means. It would be contrary to medical understanding for any compound to be able to treat generally problems, which are so different in both origin and effect. Such a thing is beyond the reach of modern medicine.

The claim sets forth the treatment of cancer generally. However, there never has been a compound capable of treating cancer generally. There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. Even the most broadly effective antitumor agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.
When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ 609. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs Novo Nordisk*, 42 USPQ2nd 1001, 1006.

Enablement for the scope of "inflammation" generally is not present. For a compound or genus to be effective against inflammation generally is contrary to medical science.

Inflammation is a process, which can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, C3a, C5a, histamine, assorted leukotrienes and cytokines, and many, many others. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally.

Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilatation and leaking of vessels, and recruitment of circulating neutrophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. They are clusters of macrophages which have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters.

Otitis media is an inflammation of the lining of the middle ear and is commonly caused by Streptococcus pneumoniae and Haemophilus influenzae. Cystitis is an inflammation

of the bladder, usually caused by bacteria. Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus. Dacryocystitis is inflammation of the tear sac, and usually occurs after a long-term obstruction of the nasolacrimal duct and is caused by staphylococci or streptococci. Preseptal cellulitis is inflammation of the tissues around the eye, and Orbital cellulitis is an inflammatory process involving the layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise from staphylococcus. Hence, these types of inflammations are treated with antibiotics.

Certain types of anti-inflammatory agents, such as non-steroidal anti-inflammatory medications (Ibuprofen and naproxen) along with muscle relaxants can be used in the non-bacterial cases. The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable to any agent to be able to treat inflammation generally.

Cardiovascular disorders embrace a vast array of problems, many of which are contradictory to others. Thus, it covers hypertension and hypotension. It covers various types of arrhythmias; angina pectoris; the thrombotic symptoms of diabetes, atherosclerosis and hyperlipoproteinaemias; ischaemic heart disease including congestive heart failure and myocardial infarction; stroke, and peripheral vascular disorders, such as deep-vein thrombosis and thrombophlebitis percutaneous transluminal coronary angiography (PTCA); elevated blood levels of triglycerides, of

total cholesterol or of LDL cholesterol; arteriosclerosis, peripheral vascular disease, cerebral vascular disease and pulmonary hypertension, migraine, cardiomyopathy, etc. Not one compound --- let alone a genus of trillions of compounds, could possibly be effective against such disorders generally.

Stroke represents one of the most intractable medical challenges. Stroke is estimated to cause about 15% of deaths, behind only heart disease and cancer. Even those who survive normally suffer from persistent damage, including motor and speech disturbances and/or convulsions. Despite a tremendous effort to resolve these problems, cerebrovascular therapy as so far been limited to trying to prevent further damage in areas on the margins of the ischemic focus, thus trying to maintain adequate perfusion in remaining intact areas, and thereby limit progressive infarction. This is generally done surgically. Standard pharmaceutical treatment, such as antiarrhythmics and antithrombotics don't get at the cause of the stroke or the damage caused, but are mostly done to insure adequate cardiac functioning.

Effective acute drug treatment of the stroke itself has so far proved to be beyond the reach of medical science. Major efforts have certainly been pressed in the area of neuroprotective therapeutics. Those studied have included use of Ca antagonists such as Levemopamil and flunarizine, to suppress neuronal calcium influx; NMDA antagonists (both competitive, such as APV and CPP, and non-competitive such as chlorpromazine, ifenprodil and Mg salts) as well as AMPA and kainate antagonists to block post-ischemic receptor-operated calcium channels; attempts to block arachidonic acid cascade or elimination of its metabolic products with agents such as lipogenase

inhibitors and thromboxane; use of free oxygen radical scavengers such as superoxide dismutase, alpha-tocopherol, or allopurinol to inhibit the lipid peroxidation that damages cell membranes, which may indirectly help prevent intracellular calcium overload; anti-edema agents such as corticosteroids; use of 5-$HT_{1A}$ receptor agonists to suppress 5-HT concentrations in the hippocampal extracellular space; use of CRF receptor antagonists to inhibit excitotoxic brain damage; use of serotonin 1A agonists such as ipsapirone, or adenosine modulators such as vinpocetine, to stimulate adenosine, which may act as a protective agent by hyperpolarizing the postsynaptic neuron; use of platelet aggregation inhibitors such as prostacycline and ticlopidine, and other approaches as well.

Despite this vast outpouring of research, the skill level in this art is sufficiently low relative to the difficulty of the task that obtaining a neuroprotective treatment of stroke was, as of the filing date, not yet possible. Hence, accomplishing such a goal involves more than routine experimentation. As evidence for this, there is cited Chalmers (TiPS Vol 17, pages 166-172 April 1996), which states flatly on page 170 that, "At present, there are no effective neuroprotective agents that can clinically ameliorate the effects of stroke in humans." Lyrer (Schweiz. Med. Wochenschr., Vol 124, #45, 2005-2012 1994) states in the summary, "Up to the present, treatment strategies for acute cerebral ischemia have not shown scientifically proven efficacy. It notes that trials on the use of cytoprotective agents "are ongoing or are planned", clear evidence of the research that remains to be done to determine how to treat stroke. For example, Pentoxifylline has been one of the most intensely studied, with dozens of studies published on its

properties. It appears to have a wide variety of effects on leucocytes, erythrocytes, neutrophils, plasma fibrinogen levels. These result in a wide ranging ability to increase blood flow, resulting in effectiveness in some vascular disorders, especially intermittent claudication. Yet, as Frampton (Drugs and Aging 7(6) 480-503 1995) notes, it is still unclear whether this drug can be made to work against stroke. Research with different administration methods, or different subcategories of stroke may well result in the discovery of how to get this drug to work, but the slowness and difficulty of this research shows clearly that this involves undue, not routine experimentation. Applicants' compounds have been subjected to far less study.

In regard to Lyme disease, it can only be treated using drugs that are antibacterial. For the human immunodeficiency virus, the only treatment available to this day are antiviral drugs. Applicants' compounds are not believed to be antiviral or antibacterial.

In regard to inflammatory bowel disease, treatment has to do with is suppression of the inflammation, but it is believed that applicants' compounds do not suppress inflammation.

Note that applicants have cancelled an ocular condition, a cardiovascular condition, a cancer and stroke from claim 120 to overcome the enablement rejection (see currently amended claim 120).

5. Claim 120 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for many of the diseases recited in claim 120, does not reasonably provide enablement for the treatment of inflammatory bowel disease, Lyme disease, human immunodeficiency virus and solid tumor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In regard to Lyme disease, human immunodeficiency virus and inflammatory bowel disease, see paragraph 4 above.

The treatment of solid tumor has been claimed. The word tumor does not always imply cancer. Some tumors (collections of abnormally growing cells) are benign (not cancerous). In discussing tumors that are malignant (cancerous), however, the term solid tumor is used to distinguish between a localized mass of tissue and leukemia. (Leukemia is actually a type of tumor that takes on the fluid properties of the organ it affects -- the blood.)

Different kinds of solid tumors are named for the type of cells of which they are composed:

**Sarcomas** -- Cancers arising from connective or supporting tissues, such as bone or muscle.

**Carcinomas** -- Cancers arising from the body's glandular cells and epithelial cells, which line body tissues.

**Lymphomas** -- Cancers of the lymphoid organs such as the lymph nodes, spleen, and thymus, which produce and store infection-fighting cells. These cells also occur in almost all tissues of the body, and lymphomas therefore may develop in a wide variety of organs.

Tumor covers cancers and neoplasms that are cancerous or not. A neoplasm is any abnormal tissue that grows by cellular proliferation more rapidly than normal, or continues to grow after the stimulus that initiated the new growth has ceased, or shows lack (partial or complete) of structural organization and/or coordination with surrounding tissue. It can be benign or malignant. Thus, such a term covers most cancers as well as precancerous conditions such as lumps, lesions, and polyps. In addition, "tumor" covers things other than neoplasms. It also covers any kind of swelling arising from inflammation. Thus, the claim would cover treatment of many kinds of inflammation. The specification cannot support that.

6. Claims 36 and 115 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. There has been recited a method of affecting hyperproliferative disorders, but the specification does not teach the method of affecting of the said disorder.

A proliferative disorder is anything that causes any abnormal tissue growth. That can be growth by cellular proliferation more rapidly than normal, or continued growth after the stimulus that initiated the new growth has ceased, or lack (partial or complete) of structural organization and/or coordination with surrounding tissue. It can be benign or malignant. Thus, such a term covers not only all cancers, but also covers precancerous conditions such as lumps, lesions, and polyps. In addition, it embraces various non-cancerous proliferative disorders such as certain types of restenosis, vascular smooth muscle proliferation associated with atherosclerosis, glomerular nephritis, clonal proliferative disorders including the various Myelodysplastic Syndromes such as Refractory anemias, certain types of abnormal wound healings, different types of abnormal angiogenisis, pulmonary fibrosis, macular degeneration, myeloproliferative disorders such as primary polycythemia and myleofibrosis, and rheumatoid arthritis. There is no such thing that an agent which is effective against such disorders generally, since they are so diverse, nor is there any reason to think that such an agent could be made to work.

When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ 609. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs Novo Nordisk*, 42 USPQ2nd 1001, 1006.

### *Claim Rejections - 35 USC § 112*

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36-37 and 120 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:

a. In claim 1 (page 4, line 6) or elsewhere in the claims, the phrase "$Z^{110}$..an optionally substituted ($C_1$-$C_6$) which.." is not clear. What is it? Is it ($C_1$-$C_6$) alkyl? Or something else? The same is true for the phrase "$Z^{105}$.. covalent bond or ($C_1$-$C_6$) which.." on page 5, line 14 and "$Z^{200}$.. substituted or unsubstituted ($C_1$-$C_6$) which.." on page 5 (lines 15-16), etc.

### *Response to arguments*

Applicant's argument filed 01/22/2004 has been fully considered but they are not persuasive.

Applicants argue the rejection by referring to page 66, lines 3-5, of the specification. Said page does not mention any ($C_1$-$C_6$) groups. Applicants only recited the number of the carbon atoms but not the nature of the groups. Applicants say that ($C_1$-$C_6$) refer to a straight chain, branched or cyclic aliphatic group that is completely saturated or having one or more units of saturation. The examiner disagrees with applicants. Said pages in the specification read as "substituted or unsubstituted benzyl,

substituted or unsubstituted benzenesulfonyl, substituted or unsubstituted phenoxy, ... substituted or unsubstituted", but this does not answer the questions raised above. Applicants also indicate in response to item 7d (Paper No. 9) that ($C_1$-$C_6$) is intended to cover "alkylene", "alkenylene" and "alkynylene", but there is nothing to support such an idea. Note that "$C_1$" is not consistent with unsaturated groups. Applicants are invited to provide guidance in the specification.

a. In claims 36, 37, the phrase "biologically active metabolites" is not clear. How can one prove that a given compound is not an "active metabolite"? It is easy to prove that a compound is biologically active metabolite, but it is not easy to prove the negative. The public has to know how to exclude biologically non-active compounds. Even if not found in blood or urine, it might have existed briefly as a metabolite.

Note that "biologically active metabolites" are cancelled from many of the claims in response to previous Office Action (e.g. see amended claim 1, claim 113, claim 120).

b. In claim 120, the term "radiation" is not a disease, but a process.

***Double Patenting***

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225

USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-34 and 36-45 and 47-88 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-86 of U.S. Patent No. 6,660,744 (Hirst et al.). Although the conflicting claims are not identical, they are not patentably distinct from each other because there is significant overlap of the invention. Note that the definitions of $R_3$, G and $R_2$ are almost the same as in the Hirst '744 with no variation at all. For example, the definition of $R^1$ = alkyl is added in the instant, but since $R^1$ is an optional substituent the of $Z^{100}$ the core chemical structure without the optional substituent is almost the same for Hirst '744 and the instant application. The definitions of $Z^{110}$, $Z^{111}$, $Z^{101}$, $Z^{102}$, Ra, and $R_1$ are exactly the same. The definition of A = -(C1-C6) is added in the instant, but the rest of the definitions are the same as Hirst '744. The definition of $R_3$ = hydrogen, hydroxy, substituted or unsubstituted alkoxy is the same for both Hirst '744 and the instant. Some definitions are added for $R_2$ in the instant application (e.g. $R_2$ = H, or E = substituted or unsubstituted alkyl), but since the definition of B = $Z^{101}$, $Z^{102}$ is the same and most of the definitions for $R_2$ are the same for the instant and Hirst '744, there is no significant changes at all. The provisos for a and b in Hirst '744 at the end of the claim

1 is the same as the instant. Note that the provisos at the end of the claim (instant application) does not exclude the species that overlap with Hirst' 744.

***Conclusion***

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kahsay Habte, Ph. D. whose telephone number is (571) 272-0667. The examiner can normally be reached on M-F (9.00AM- 5:30PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on (571) 272-0674 or if there is no response within 24 hours call James Wilson on (571)272-0661. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Kahsay Habte, Ph. D.
Examiner
Art Unit 1624

Mark L. Berch
Primary Examiner
Art Unit 1624

KH
February 17, 2004